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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,341	09/24/2001	Erwin Mattes	P-204.00 CON	2148

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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,341	MATTES ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-73* is/are pending in the application.

4a) Of the above claim(s) *10-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/963,341.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group IV, claims 59-73, in the reply filed on 7/15/04 is acknowledged.

Claims 10-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/15/04. In the reply filed on 7/15/04, Applicant states that the claims set forth in Groups II and III were cancelled without prejudice in the first preliminary amendment date 9/24/01. A review of the first preliminary amendment shows that claims 1-9 were cancelled and claims 10-56 were added. There was no cancellation of claims corresponding to Groups II (29-54) or III (55-58).

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 63-66 recite the limitation "starting material" in the first line of each said claim. There is insufficient antecedent basis for this limitation in claim 59.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 59-64, 66 and 69-71 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chan et al. (FEBS Lett. (1973) 35(1): 79).

Chan et al. disclose the purification of human α1-antityrpsin (α1-AT). Serum from an individual having normal homozygous α1-AT was purified by gel chromatography on Sephadex. This disclosure meets the limitation of claim 63 because serum is a plasma fraction. The eluant from the gel chromatography was passed through an anion exchange resin, DEAE-cellulose. This step was repeated until all of the albumin had been removed from the desired α1-AT (p. 79, right column). The albumin free fractions were then subjected to further purification on Bio-Gel hydroxyapatite (HAP) supplied by Bio-Rad with a linear gradient from 0.005 M-0.3 M (which corresponds to a convention range of 5 mM-300 mM; p. 90. left column, bottom of page) of potassium phosphate buffer at pH 6.5, which satisfies the pH buffer limitations of claims 61 and 62. After this step, the α1-AT fraction was again subjected to anion exchange chromatography to remove any lingering traces of albumin. Chan et al. report that the purified α1-AT migrated as a single band on polyacrylamide gel-electrophoresis and that a complete carbohydrate and amino acid composition showed that the purified α1-AT was unaltered by a purification process (p. 80, right column and Table 1, p. 81). Therefore, Chan et al. disclose a homogenous, purified, unaltered α1-AT that was obtained by a process that is substantially the same as the claimed purification method. Therefore, the purified α1-AT disclosed by Chan et al. is inherently the same as that disclosed by the instant specification. The claimed pI claimed does not make the instant claims patentable over the prior art because the pI of the purified α1-AT is an inherent property of the molecule.

> MPEP 2112.02: PROCESS CLAIMS - PRIOR ART DEVICE ANTICIPATES A CLAIMED PROCESS IF THE DEVICE CARRIES OUT THE PROCESS DURING
> Under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. When the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process. In re King, 801 F.2d 1324, 231USPQ 136 (Fed. Cir. 1986) See also In re Best, 562F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) Ex parte Novitski, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993

Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

It is noted that the claim language is open ("comprising"). Therefore, disclosure which teaches extra step that are not recited in a claim still meet the claim. For example, claim 59 only recites only the step of chromatography on HAP. The disclosure of Chan et al. meets the limitations of claim 59 even though Chan et al. disclose extra steps not recited in claim 59. The anion exchange step taught by Chan et al. meets the limitation of claim 60 that further requires purification by anion exchange. Claim 60 does not specify an order to the anion exchange and HAP chromatography (i.e. anion exchange is first). However, the disclosure by Chan et al. meets either order of steps (i.e. HAP chromatography followed by anion exchange, or the reverse) since an anion exchange chromatographic step occurs both before and after the purification on HAP.

Claim 64 and 66 require that the "starting material" is albumin-depleted (cl. 64) and "pre-purified" (cl. 66). The broadest reasonable interpretation of "starting material" is the material to be purified at any point in the purification scheme. Thus, each step of the purification requires a "a starting material." The limitations of claim 64 are met because the starting material for the HAP column step comprises α1-AT that that has a reduced amount of albumin since it had been subjected to anion exchange chromatography. The broadest reasonable interpretation of the limitation "pre-purified" is that the material has undergone some degree of purification prior to the next step of the procedure. Therefore, said starting material for the HAP column was pre-purified since it had all ready undergone a purification step on the anion exchange column. The prior art disclosure meets the claim limitations

regarding ionic strength (equivalent to 60 mM (cl. 69), 40 mM (cl. 70) or 50 to 130 mM of phosphate (cl. 71)) because all of the claimed phosphate buffer concentrations fall within the phosphate buffer gradient disclosed by Chan et al. (5 to 300 mM). During the gradient elution, the concentration of the phosphate will run between 5 and 300 mM and thus, include the claimed values.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Bio-Rad Catalog (website) and Fitchmun (US 5,760,179).

The disclosure of Chan et al. is discussed *supra*.

Chan et al. do not teach the employment of ceramic HAP for the disclosed α1-AT purification method.

The Bio-Rad Catalog teaches that Bio-Gel HAP, which was used by Chan et al., is a crystalline HAP suitable for the purification of proteins, nucleic acid ad other macromolecules. The Bio-Rad Catalog also discloses CHT ceramic HAP (formerly known as Macro-Pep) is a spherical macroporous form of HAP that overcomes the limitations of crystalline HAP. It can be used for several hundred purification cycles, it has a higher protein binding capacity for acidic proteins and a very low affinity for albumin.

Fitchmun discloses that Macro-Prep ceramic HAP (col. 2, lines 45-49) was provided by Bio-Rad laboratories at least by 1996 (filing date of the patent). Fitchmun is cited to show that Bio-Rad supplied ceramic HAP at the time the instant invention was made.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the crystalline Bio-Gel HAP with a ceramic HAP in the purification method taught by Chan et al. The ordinary artisan would have been motivated to make this substitution because ceramic HAP has a higher binding capacity for acidic proteins and less affinity for albumin. This would have been advantageous to the purification taught by Chan et al. because α1-AT is an acidic protein and would benefit from greater binding capacity. Also, the ceramic HAP would be more effective in ridding the α1-AT of contaminating albumin. The ordinary artisan would have had a reasonable expectation that α1-At could be purified on ceramic HAP because Bio-Rad advises that separation protocols developed on crystalline HAP can be transferred directly to the ceramic material with little or no modification (first paragraph of product information).

Claims 65, 67 , 72 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Lebing et al. (US 5,610,285).

The disclosure of Chan et al. is discussed supra.

Chan et al. do not teach using a Cohn fraction of blood as a starting material for the purification. Neither do Chan et al. disclose the employment of a detergent or heat to inactivate pathogens present in the preparation.

Lebing et al. teach the purification of α1-AT from a paste suspension of Fraction IV-1 (equivalent to Fraction IV A) which is derived from plasma. This meets the limitation of claim 65 for a Cohn V starting material because the specification states that a Cohn IV A fraction is substantially the same as a Cohn V precipitate (p. 16, 2nd paragraph of the instant specification). Lebing et al. teach that it is important to inactivate viral pathogens that may be present in the plasma by adding a detergent to the chromatography or employing a dry heat or pasteurization step to the method (col. 3, lines 40-55 of the referenced patent).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a Cohn IV A plasma fraction as a source of α1-AT and to employ a detergent in the chromatography in the method taught by Chan et al. The ordinary artisan would have been motivated to use the Cohn IV A fraction because it is readily available and is well known as a source of alph1-AT. The ordinary artisan would have been further motivated to employ a detergent or a heat step in order to inactivate any pathogens that may contaminate the donor plasma source and thereby render unusable for pharmaceutical purposes any purified α1-AT from said source. The ordinary artisan would have had a reasonable expectation that α1-At could be obtained from the disclosed plasma fractions and that detergent could inactivate viral blood pathogens because Lebing et al. demonstrated that said source and pathogen inactivation were readily accomplished.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEAN C. WITZ
PRIMARY EXAMINER